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Inspiratory muscle training in patients with cystic fibrosis

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Little information is available about the effects of inspiratory muscle training in patients with cystic fibrosis (CF). In this study the effects of inspiratory-threshold loading in patients with CF on strength and endurance of the inspiratory muscles, pulmonary function, exercise capacity, dyspnoea and fatigue were evaluated.

Sixteen patients were assigned to one of two groups using the minimization method: eight patients in the training group and eight patients in the control group.The training was performed using an inspiratory-threshold loading device. Patients were instructed to use the threshold trainer 20 min a day, 5 days a week for 6 weeks. Patients in the training group trained at inspiratory threshold loads up to 40% of maximal static inspiratory pressure (Pimax) and patients in the control group got 'sham' training at a load of 10% of Pimax. No significant differences were found among the two groups in gender, age, weight, height, pulmonary function, exercise capacity, inspiratory-muscle strength and inspiratory-muscle endurance before starting the training programme. Mean (SD) age in the control group was 19 (5·5) years, mean (SD) age in the training group was 17 (5·2) years. Mean FEV_1 in both groups was 70% predicted, mean inspiratory-muscle strength in both groups was above 100% predicted.

All patients except one, assigned to the training group, completed the programme. After 6 weeks of training, mean inspiratory-muscle endurance (% Pimax) in the control group increased from 50% to 54% ($P=0{\cdot}197$); in the training group mean inspiratory muscle endurance (% Pimax) increased from 49% to 66% ($P=0{\cdot}003$). Statistical analysis showed that the change in inspiratory-muscle endurance (% Pimax) in the training group was significantly higher than in the control group ($P=0{\cdot}012$). After training, in the training group there was a tendency of improvement in Pimax with an increase from 105 to 123% predicted, which just fell short of statistical significance ($P=0{\cdot}064$). After training no significant differences were found in changes from baseline in pulmonary function, exercise capacity, dyspnoea and fatigue. It is concluded that low-intensity inspiratory-threshold loading at 40% of Pimax was sufficient to elicit an increased inspiratory-muscle endurance in patients with CF.

Key words: cytic fibrosis; inspiratory muscle training; inspiratory threshold; inspiratory muscle strength; inspiratory muscle endurance; pulmonary function.

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Introduction

Cystic fibrosis (CF) is a complex disease which affects multiple organ systems and thereby physiological functions. Patients often suffer from impaired pulmonary function, impaired exercise capacity and poor nutritional status. Whether dysfunction of inspiratory-muscle strength is present in CF patients is controversial. A preserved inspiratory muscle strength has been reported in previous studies (1,2,3,4), suggesting an inspiratory-muscle training effect caused by airway obstruction. Lands *et al.* (5) suggested that CF patients in a later stage of the disease are not able to maintain their inspiratory muscle strength. Other authors (6,7) also found reduced inspiratory-muscle strength in CF patients. Lack of efficiency of the inspiratory muscles, as a result of malnutrition (3) and hyperinflation (6), may lead to development of inspiratory-muscle fatigue and therefore dyspnoea.

It is thought that specific inspiratory-muscle training may forestall inspiratory-muscle fatigue and therefore delay dyspnoea. Most of the previous studies evaluating the effects of inspiratory-muscle training were performed in patients with chronic obstructive pulmarary disease (COPD) and concerned inspiratory-resistive training and more recently inspiratory-threshold loading.

In CF patients, Keens *et al.* (8) showed that specific normocapnic hyperpnoea training improved ventilatory-muscle endurance. Asher *et al.* (9) demonstrated increases in strength and endurance of inspiratory muscles, but no improvement in exercise capacity after twice daily 15-min sessions during 4 weeks of inspiratory-muscle training at a

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maximal possible resistance in 11 CF patients. Sawyer *et al.* (10) compared 10 children with CF who underwent inspiratory-threshold training at loads up to 60% of maximal static inspiratory pressure (Pimax) 30 min daily for 10 weeks with a control group of 10 CF children who received 'sham' training. The experimental group showed significant improvement in inspiratory-muscle strength, pulmonary function and exercise capacity.

Apparently, there is a tendency to improve endurance and strength of the inspiratory-muscles as well as exercise capacity, after inspiratory-muscle training at high intensity in CF patients. Whether inspiratory-muscle training at lower intensity would be beneficial in CF patients has not been determined yet. Furthermore, less information is available about the effects of inspiratory-muscle training on subjective outcome variables. Therefore, the purpose of this study was to evaluate the effects of inspiratory-threshold loading at low intensity in patients with CF on strength and endurance of the inspiratory muscles, pulmonary function, exercise capacity, dyspnoea and fatigue.

Methods

PATIENTS

Patients with CF ($n=16$), ranging in age from 10 to 25 years, were recruited on the basis of their willingness to take part in this study. Clinical characteristics are given in Table 1. Written informed consent was obtained from the patients or parents. The study was approved by the Medical Ethics Committee of the University Hospital.

Patients were assigned to one of two groups by five patient factors: gender; age; FEV_1; FVC; and body mass index using the minimization method (11). Eight patients in the experimental group trained at inspiratory-threshold loads up to 40% of Pimax (training group) and eight patients received 'sham' training at a minimal pressure load of 10% of Pimax (control group).

In both groups, the following variables were measured at baseline and after 6 weeks of training:

Pulmonary function

Inspiratory vital capacity (IVC), FVC and FEV_1 were measured using body plethysmography (Jaeger, System 2800, Germany). Predicted values of Quanjer *et al.* were used to express pulmonary function as a percentage of the predicted value (12). Residual volume (RV) and total lung capacity (TLC) were only measured at baseline to characterize patients. The RV/TLC ratio (% predicted) was calculated.

Exercise capacity

Exercise capacity was assessed using an automatic electro-magnetically braked bicycle (Jaeger EOS sprint, Germany) during continuous ECG recording. Each subject exercised continuously (pedal speed: 60 rpm) with an initial workload of 0 Watt for 1 min, which was increased every minute by 10 Watts. HR, BF, VE, VO_2 and VCO_2 were recorded for 5 min at baseline and throughout the exercise test. The test was terminated when exhaustion was apparent or earlier, at the physician's discretion, when physiological endpoints (i.e. decline in blood pressure, ECG changes, attainment of theoretically maximal heart rate) were exceeded (13). The maximal workload was defined as the highest load which could be reached and maintained for at least 0·5 min.

TABLE 1. Characteristics of the patients at baseline (mean SD values)

	Control group ($n=8$)	Training group ($n=8$)	P-value
Gender (M/F)	4/4	4/4	
Age, years	19 (5·5)	17 (5·2)	0·552
Height, cm	169 (13)	167 (15)	0·724
Weight, kg	54·6 (12)	50 (13)	0·477
FEV_1, l	2·46 (1·24)	2·34 (0·74)	0·823
FEV_1, % pred.	70 (29)	70 (25)	0·993
FVC, l	3·30 (1·08)	3·28 (1·19)	0·984
FVC, % pred.	80 (20)	81 (21)	0·895
FEV_1/IVC, %	67·5 (17·4)	68·5 (12·5)	0·905
RV, l	1·81 (1·33)	2·08 (0·99)	0·655
TLC, l	5·21 (1·42)	5·44 (1·82)	0·787
RV/TLC, % pred.	119 (32)	137 (32)	0·569
Wmax, % pred.	72 (20)	69 (13)	0·768
IMS, % pred.	129 (32)	106 (21)	0·113
IME, % Pimax	50 (5)	48 (12)	0·590

IMS: inspiratory muscle strength;
IME: inspiratory muscle endurance; Pimax; maximal static inspirator pressure;
P-value: t-test for unpaired samples.

Maximum exercise capacity (Wmax) expressed as the percentage of the predicted maximum exercise capacity using the equation of Wasserman *et al.* (14) was used for analysis. Before exercise and during the last 10 sec of each work level patients were asked to rate the subjective degree of dyspnoea using the modified Borg-scale (15). This category scale is an indicator of the intensity of dyspnoea. The scale ranges from 0 to 10 where a value of 0 represents 'nothing at all' and a value of 10 denotes that the intensity of dyspnoea is maximal. The Borg-scale was shown to patients printed on a sheet of paper after a standard set of instructions (16).

Inspiratory muscles

Strength. Inspiratory-muscle strength was assessed by measuring Pimax at RV with a portable Pmax Monitor (P.K. Morgan Ltd., England). The manoeuvre was repeated until a reproducible pressure plateau was seen. The highest recorded pressure maintained for 1 sec was taken for analysis. Values were expressed in cm H_2O. Normal values of Wilson *et al.* (17) were used to determine the percentage of predicted values.

Endurance. To determine inspiratory-muscle endurance, a commercially-available threshold-loading device (Threshold, Healthscan Products, Inc. U.S.A.) was used during an incremental loading procedure (18,19). In order to obtain pressures over 41 cm H_2O an additional spring was inserted with a double-spring constant, as described by Gosselink *et al.* (20). Patients started inspiring from a threshold-loading device set at 30% of Pimax for 2 min. The threshold load was then increased every 2 min in increments of 10% of Pimax. The maximal load was defined as the highest load which could be reached and maintained for at least 1 min as a percentage of Pimax. The breathing pattern was not regulated. Before assessment and during the last 10 sec of each load-level, patients were asked to rate the subjective degree of dyspnoea using the modified Borg-scale.

Training. The training was performed using the threshold-loading device, which has been found to be reliable and reproducible for loading inspiratory muscles (20).

Patients were instructed to use the threshold trainer 20 min a day, 5 days a week, for 6 weeks. Patients of both groups were asked to continue their normal life-style during this period, except for completing the prescribed, unsupervised, daily inspiratory-muscle training. Patients in the training group started to train at a resistance of 20% of their Pimax, for 1 week. The resistance was then increased to 30% of Pimax in the second week and to 40% of Pimax for the last 4 weeks. Patients in the control group breathed through the threshold trainer with an inspiratory resistance of 10% of Pimax. This low resistance could be considered as 'sham' training, according to recommendations of Reid *et al.* (21) that inspiratory-muscle-training intensity should be minimally 30% of Pimax to obtain effects.

Questionnaires

Patients also completed the following questionnaires at baseline and at the end of the study:

Subjective fatigue. To determine subjective fatigue the Fatigue Index 20 (MFI-20) was developed by Smets *et al.* (22,23) and used in our study. The psychometric properties of the MFI-20 have been evaluated in cancer patients, patients with Chronic Fatigue Syndrome, psychology students, medical students, army recruits and junior physicians (22). The MFI-20 has established construct and convergent validity and shows good internal consistency. The MFI-20 contains 20 positive- and negative-directed statements that deal with five dimensions of fatigue, four statements per dimension. Patients are asked to rate their condition according to the last days. Each answer consists of an ordinal scale ranging from 'yes, that's correct' (score 1) to 'no, that's incorrect' (score 5). Scores range from 1 to 5. A higher score implies more severe fatigue. A score for each dimension is calculated by summation of the scores for each question per dimension. This score can be a minimum of 4 and a maximum of 20. Likewise a higher score implies more severe subjective fatigue.

MRC dyspnoea. The Dutch version of the Medical Research Council (MRC) dyspnoea scale was used to rate limitation in function due to dyspnoea (24). This scale is based on six grades with regard to dyspnoea during physical activities and during rest. To grade dyspnoea with the MRC scale, patients were interviewed by asking questions concerning the patient's symptoms according to the instructions reported by Van der Lende *et al.* (25). A higher MRC grade indicates more impairment due to dyspnoea.

STATISTICAL ANALYSES

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS-version 7·5). Values are presented as means (SD).

Differences in recorded variables between the two groups at baseline were analysed using Student's *t*-test for unpaired samples. The *t*-test for paired samples was used to compare pre- and post-training values within each group. For each individual patient the absolute change from baseline after the intervention (training or sham) was calculated for all variables. Differences in change from baseline between the training and the sham training group were analysed using the *t*-test for unpaired samples. A *P*-value lower than 5% was considered as statistically significant.

Results

All patients except one, assigned to the training group, completed the programme. This patient stopped the programme because of earache during inspiratory-threshold training with a load of 40% of Pimax. Also, this patient

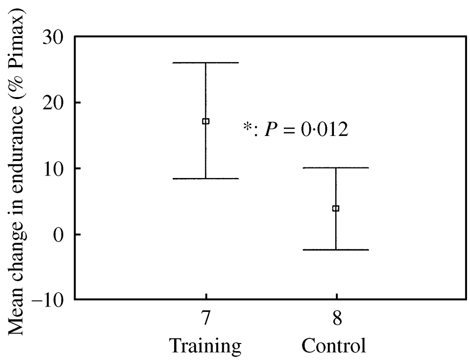

FIG. 1. Mean change in inspiratory muscle endurance (% Pimax—maximal static inspiratory pressure) in training group and control group

did not perform the assessments at the end of the programme and was excluded from statistical analysis of the data of the training period. There were no significant differences among the two groups in gender, age, weight, height, pulmonary function, exercise capacity, inspiratory-muscle strength and inspiratory-muscle endurance before starting the training programme (Table 1). Mean FEV_1 in both groups was 70% predicted. Mean inspiratory-muscle strength in the control as well as in the training group was above 100% predicted. Mean inspiratory-muscle endurance in both groups was around 50% of Pimax value.

After 6 weeks of training, mean inspiratory-muscle endurance (% Pimax) in the control group increased from 50% to 54% ($P=0{\cdot}197$). In the training group, mean inspiratory-muscle endurance (% Pimax) increased significantly from 49% to 66% ($P=0{\cdot}003$). Analysis showed that the change in inspiratory muscle endurance (% Pimax) in the training group was significantly higher than in the control group ($P=0{\cdot}012$) (Figure 1). Concerning all other physiologic variables, after 6 weeks of training no significant within group differences and no significant differences in changes from baseline between the groups (Table 2) were found. According to Borg- and MRC-dyspnoea scores, and subjective Fatigue scores after training, no significant within group differences and no significant differences in changes from baseline between the groups (Table 3) were found.

Discussion

In the present study it was found that inspiratory-threshold loading 20 min a day, 5 days a week during 6 weeks significantly improved inspiratory-muscle endurance, but not inspiratory-muscle strength, pulmonary function, exercise capacity, dyspnoea and fatigue in CF patients.

The finding that inspiratory muscle training leads to an increased endurance capacity of the inspiratory muscles is in agreement with the results of Asher *et al.* (9). However, in contrast with the finding of the present study, Asher *et al.* also found an improved inspiratory-muscle strength after their training programme. Sawyer *et al.* (10) found increased strength of the inspiratory muscles, but did not report endurance capacity. It is unlikely that differences between these outcomes and the result of the present study can be explained by differences in initial Pimax values (% predicted) before training. In the study by Sawyer and in the present study Pimax was well preserved, with values

TABLE 2. Physiologic variables (mean SD values)

	Control			Training			Change from baseline between control and training
	Pre ($n=8$)	Post ($n=8$)	P-value	Pre (n7)	Post ($n=7$)	P-value	P-value
FEV_1 (l)	2·46 (1·24)	2·56 (1·09)	0·565	2·27 (0·77)	2·33 (0·71)	0·268	0·822
FEV_1 (% pred.)	70 (29)	73 (29)	0·604	72 (27)	70 (21)	0·541	0·460
FVC (l)	3·30 (1·08)	3·33 (0·95)	0·828	3·03 (1·02)	3·07 (0·90)	0·703	0·999
FVC (% pred.)	80 (20)	80 (21)	0·934	80 (22)	79 (18)	0·699	0·789
Wmax (W)	125 (48)	126 (48)	0·685	111 (48)	106 (44)	0·172	0·166
VO_2 max (ml $kg^{-1}min^{-1}$)	33 (10)	30 (11)	0·082	33 (8)	29 (6)	0·171	0·995
VEmax (l/min)	59 (25)	58 (20)	0·845	45 (17)	40 (15)	0·095	0·347
Pimax (% pred.)	129 (32)	139 (36)	0·103	105 (23)	123 (21)	0·064	0·401
IME (%Pimax)	50 (5)	54 (7)	0·197	49 (12)	66 (14)	0·003*	0·012**

IME: inspiratory muscle endurance; Pimax: maximal static inspiratory pressure;
*significant difference between pre- and postvalue in the control group or training group analysed using the t-test for paired samples;
**significant difference in change from baseline between the training and the control group analysed using the t-test for unpaired samples.

TABLE 3. Subjective variables (mean SD values)

	Control			Training			Change from baseline between control and training
	Pre ($n=8$)	Post ($n=8$)	P-value	Pre ($n7$)	Post ($n=7$)	P-value	P-value
Borgmax, endurance	1·0 (1·8)	1·0 (1·8)	0·305	1·4 (1·2)	1·3 (1·3)	0·220	0·603
Borgmax, bicycle	4·2 (3·3)	4·5 (3·3)	0·551	5·3 (2·7)	4·3 (3·5)	0·263	0·197
MFI-GF	6·63 (3·70)	8·00 (4·56)	0·390	7·57 (4·50)	6·43 (2·76)	0·364	0·208
MFI-PF	7·88 (5·30)	7·75 (4·68)	0·802	6·71 (3·90)	6·57 (4·24)	0·805	0·981
MFI-RA	6·88 (4·36)	8·25 (5·29)	0·181	5·14 (1·22)	6·57 (1·99)	0·065	0·960
MFI-RM	5·00 (1·41)	8·38 (5·18)	0·073	5·14 (1·46)	5·00 (1·53)	0·859	0·076
MFI-MF	6·38 (3·20)	9·75 (5·68)	0·185	6·57 (1·51)	7·29 (2·56)	0·376	0·301
MRC dyspnoea	0·63 (1·06)	0·50 (0·76)	0·351	0·43 (0·79)	0·33 (0·82)	0·541	0·351

Borgmax, endurance: Borg score at maximal work load during inspiratory-muscle endurance test;
Borgmax, bicycle: Borg score at maximal work load during bicycle ergometry test;
MFI-GF: Multidimensional Fatigue Inventory-General Fatigue score;
MFI-PF: Multidimensional Fatigue Inventory-Physical Fatigue score;
MFI-RA: Multidimensional Fatigue Inventory-Reduced Activity score;
MFI-RM: Multidimensional Fatigue Inventory-Reduced Motivation score;
MFI-MF: Multidimensional Fatigue Inventory-Mental Fatigue score;
MRC dyspnoea: Medical Research Council dyspnoea scale.

Differences between pre- and post-value within the control group and within the training group were analysed using the t-test for paired samples.
Differences in change from baseline between the training and the control group were analysed using the t-test for unpaired samples.

above 100% predicted. However, there are important differences between the studies in intensity and duration of the inspiratory-muscle training programmes. Asher trained patients twice daily with 15 min each session on maximal possible resistance. Sawyer applied inspiratory-threshold loadings up to 60% Pimax for 10 weeks, 30 min a day. Intensity of the present training programme was much lower, with loads up to 40% of Pimax in the training group. It has been suggested that low-intensity training results in improvement in inspiratory-muscle endurance and that high-intensity training specifically improves inspiratory-muscle strength (21,26). This may explain the fact that the authors only found an effect on inspiratory-muscle endurance and not on inspiratory-muscle strength.

In addition, it should be noted that in the present study after training patients in the training group showed a tendency of improvement in Pimax (from 105 to 123% predicted), which just fell short of statistical significance ($P=0·064$). The lack of significant improvement in Pimax might be related to the relatively small number of patients presented in our training group ($n=7$) as compared to the studies of Asher *et al.* ($n=11$) and Sawyer *et al.* ($n=10$). The improvement in Pimax might have been statistically significant had more patients been tested. Endurance capacity of the inspiratory muscles in the present group of patients was lower than described in elderly persons and non-elderly asymptomatic persons (19). It has been shown that 'normal' endurance is around 80%, while the CF patients in the present study had an endurance of only 50% prior to the training. The improvement to 66% in the training group was significant, but the endurance remained lower than normal. The increased inspiratory-muscle endurance in the present study did not result in transfer effects like increased pulmonary function, exercise capacity, reduced dyspnoea or less fatigue as was hypothesized beforehand. This finding confirms the results of Asher *et al.* (9), who found no effect of inspiratory-muscle training on exercise capacity in CF patients. In contrast, Sawyer *et al.* (10) found an increased exercise capacity measured as endurance on a treadmill. Surprisingly, in this study improvement in pulmonary function was found in the inspiratory-muscle training group. The reason for the improvement in pulmonary function in the study of Sawyer is not clear and could not be confirmed by this study. Redline *et al.* (27) found that in healthy subjects inspiratory-muscle training resulted in increased muscle strength but also reduced sensation of inspiratory effort. This could not however be confirmed in the present study.

Moreover, it was found that functional status as measured by the MRC scale and the MFI-20 questionnaire did not improve due to inspiratory-muscle training.

In conclusion, low-intensity inspiratory-threshold loading leads to an increased inspiratory-muscle endurance in these particular CF patients. Further studies involving larger numbers of patients are required in order to clarify whether low-intensity inspiratory-muscle training could elicit significant improvements in Pimax. Furthermore, research is needed to determine the specific and transfer effects of inspiratory-muscle training in patients with CF.

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